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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of:

Nisson et al.

Appl. No. 09/829,066

Filed: April 10, 2001

For: **Method for Isolating and Recovering Target DNA or RNA Molecules Having a Desired Nucleotide Sequence**

Confirmation No.: 1532

Art Unit: 1656

Examiner: *To be assigned*

Atty. Docket: 0942.4800002/RWE/ALS

Second Preliminary Amendment and Submission of Substitute Sequence Listing Under 37 C.F.R. § 1.825(a)

Commissioner for Patents
Washington, D.C. 20231

Sir:

This Amendment is provided in the following format:

(A) A clean version of each replacement paragraph/section/claim along with clear instructions for entry;

(B) Starting on a separate page, appropriate remarks and arguments. 37 C.F.R. § 1.111 and MPEP 714; and

(C) Starting on a separate page, a marked-up version entitled: "Version with markings to show changes made."

It is not believed that extensions of time or fees for net addition of claims are required beyond those that may otherwise be provided for in documents accompanying this paper. However, if additional extensions of time are necessary to prevent abandonment of this application, then such extensions of time are hereby petitioned under

37 C.F.R. § 1.136(a), and any fees required therefor (including fees for net addition of claims) are hereby authorized to be charged to our Deposit Account No. 19-0036.

Amendments

In the Specification:

Please substitute the following paragraphs/sections for the pending paragraphs/sections.

Please substitute the first full paragraph on page 37 with the following paragraph:

C1

Oligonucleotide D1024 (GTN TG(T/C) GA(T/C) GGN TT(T/C) CA(T/C) GTN GG) (Seq ID NO 1) has a degeneracy of 1024. The sequence in which dK is substituted for the A/G degenerate position, dP for the C/T degenerate position and dP/dK for all four nucleotides is given by GT(dP/dK) TG(dP) GA(dP) GG(dP/dK) TT(dP) CA(dP) GT(dP/dK) GG (Seq ID NO 12). The sequences represented by oligonucleotide D1024-PK, which has a degeneracy of 8, are depicted in Table 3.

Please substitute the paragraph beginning on page 40, line 4 with the following paragraph:

C2

In another embodiment of the present invention, the present invention may be used to preferentially isolate cDNA molecules that contain the 5' terminus including the translation initiation codon. This is accomplished by developing degenerate

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oligonucleotide to the Kozak sequence which includes the translation initiation codon and extends 5' approximately 13 nucleotides (Kozak, M, *Nucleic Acids Res. 8*:125-32 (1987); Kozak, M, *J. Biol. Chem 266*:19867-70 (1991)). The consensus sequence for initiation of translation by eukaryotic ribosomes is GCC GCC (A/G)$^{-3}$CC A^{1}UG G^{4} (SEQ ID NO 11), Kozak, M, *Nucleic Acids Res. 8*:125-32 (1987); Kozak, M, *J. Biol. Chem 266*:19867-70 (1991), herein incorporated by reference; Sambrook *et al.*, 16.16, In *Molecular Cloning, a Laboratory Manual*, Cold Spring Harbor Press (1989), herein incorporated by reference. Two approaches can be attempted to enrich for the presence of the 5' terminus including the translation start codon. In the first, the degenerate Kozak oligonucleotide probe can be used to enrich by GeneTrapper for 5' sequences followed by the use of a gene-specific GeneTrapper probe. Alternatively, a gene-specific GeneTrapper probe can be applied to a phagemid cDNA library using GeneTrapper followed by the use of a degenerate Kozak oligonucleotide probe. In both cases, the percentage of clones that contain the 5' terminus including the translation initiation codon should be enriched. This method will be especially useful for clones derived from longer mRNAs (i.e., greater than 5 Kb).

In compliance with 37 C.F.R. § 1.825(a), Applicants submit substitute sheets to amend the paper copy of the Sequence Listing. Please cancel the existing Sequence Listing for the above-identified application, replace it with the substitute Sequence Listing appended hereto, and insert the same at the end of the application.

Remarks

This is responsive to the Notice to Comply with Requirements for Patent Applications Containing Nucleotide Sequence and/or Amino Acid Sequence Disclosures, mailed May 29, 2001, a copy of which is provided herewith.

Upon entry of the foregoing amendment, claims 1-4 and 6-71 are pending in the application, with claims 1, 9 and 42 being the independent claims.

Support for the addition of SEQ ID NO:12 can be found, for example, on page 36, lines 10-16 and on page 37 in the first paragraph and Table 3. SEQ ID NO:12 merely rephrases the subtantive information of Table 3. In particular, Table 3 describes 8 different sequences with variations only in positions 3, 12 and 21. These positions must be either dK or dP. Likewise, SEQ ID NO:12 describes these 8 different sequences. "Mere rephrasing of a passage does not constitute new matter." M.P.E.P. § 2163.07 (I). Other changes to the specifcation are to correct obvious typographical errors. These changes are believed to introduce no new matter, and their entry is respectfully requested. See M.P.E.P. §2163.07 (II).

Applicants' Agent hereby states that the change made in the sequence listing does not include new matter. Applicants' undersigned agent has amended the specification to direct the entry of this corrected Sequence Listing at the end of the application.

In accordance with 37 C.F.R. § 1.825(b), the paper copy of the Sequence Listing and the computer readable copy of the Sequence Listing submitted herewith are the same.

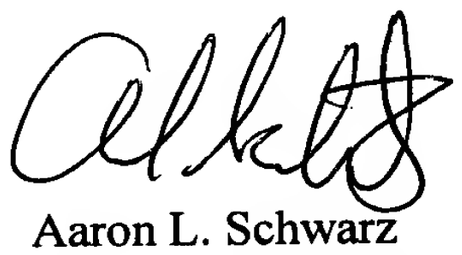
Conclusion

If the Examiner believes, for any reason, that personal communication will expedite prosecution of this application, the Examiner is invited to telephone the undersigned at the number provided.

Prompt and favorable consideration of this Amendment is respectfully requested.

Respectfully submitted,

STERNE, KESSLER, GOLDSTEIN & FOX P.L.L.C.



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